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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,866	09/26/2003	C. Frank Bennett	RTS-0242US.P1	2637

55389 7590 03/07/2006

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,866	BENNETT ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alignment*.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 12/28/205 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 05/03/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 12/28/2005, claims 1-9 and newly added claims 11-12 are currently under examination in the instant application. Applicant has canceled claim 10.

Applicant's arguments with respect to claims 1-9 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

Applicant has requested the rejection be held in abeyance until allowable matter is indicated in a least one of the cases.

Therefore, the rejection of claims 1-9 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-2, 4-10 and 15 of copending Application No. 10/633,843 is maintained for the reason of record.

Information Disclosure Statement

It was noted that reference AP was not initialed on sheet 4 of 4 in the PTO-1449 filed 05/03/2005. The reference has been considered and the PTO-1449 is initialed and placed in the file.

New Rejections

Claim Rejections - 35 USC § 102 or 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 11 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Stinchcomb et al. (Patent No: 6,194,150).

The instant claims are drawn to a compound 8 to 50 nucleobases in length targeted to the nucleobases 436-477 of a nucleic acid molecule (SEQ ID NO: 3) encoding human superoxide dismutase 1, soluble wherein the compound specifically hybridizes with and inhibits expression

of human superoxide dismutase 1 and wherein the compound is an antisense compound, wherein the antisense oligonucleotide comprises a modified phosphorothioate linkage, a 2'-O-methoxyethyl sugar moiety or a modified nucleobase.

Stinchcomb et al. teach a compound, 15 nucleobases in length (SEQ ID NO: 2103) targeted to nucleobases 431-442 of the instant nucleic acid molecule (SEQ ID NO: 3) encoding human superoxide dismutase 1, soluble (see attachment of sequence alignment). Stinchcomb et al. teach antisense oligonucleotide comprises a 2'-O-methoxyethyl sugar moiety (see column 11, lines 35-40) and further comprises base modifications (column 9, lines 40-64 and claim 20) or phosphorothioate linkages (see claim 22). The nucleic acid sequence taught by Stinchcomb et al. meets the structural limitation of claims 1-7 and 11 of the instant application and would be expected to specifically hybridize to a nucleic acid encoding of human superoxide dismutase 1, soluble. Furthermore, since the prior art antisense compound meets all the structural limitations of the claims, the prior art antisense would then be considered to "inhibit expression" of the gene as claimed, absent evidence to the contrary. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic.

Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Thus, the instant claims are anticipated or obvious over Stinchcomb et al.

Claim 12 is rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Chenchik et al. (Patent No: 6,352,829).

The instant claims are drawn to a compound 8 to 50 nucleobases in length targeted to the nucleobases 452-471 of a nucleic acid molecule (SEQ ID NO: 3) encoding human superoxide dismutase 1, soluble wherein the compound specifically hybridizes with and inhibits expression of human superoxide dismutase 1, soluble.

Chenchik et al. teach a compound, 40 nucleobases in length (SEQ ID NO: 2103) targeted to nucleobases 464-503 of the instant nucleic acid molecule (SEQ ID NO: 3) encoding human superoxide dismutase 1, soluble (see attachment of sequence alignment). The nucleic acid sequence taught by Chenchik et al. meets the structural limitation of claim 12 of the instant application and would be expected to specifically hybridize to a nucleic acid encoding of human superoxide dismutase 1, soluble. Furthermore, since the prior art antisense compound meets all the structural limitations of the claims, the prior art antisense would then be considered to "inhibit expression" of the gene as claimed, absent evidence to the contrary. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C.

102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Thus, the instant claim is anticipated or obvious over Chenchik et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stinchcomb et al. (Patent No: 6,194,150), in view of Baracchini (U.S. Patent NO: 5,80,1154) and in further view of Bennett et al. (U.S. Patent NO: 6,077,833).

The instant claims are drawn to a compound 8 to 50 nucleobases in length targeted to the nucleobases 436-477 of a nucleic acid molecule (SEQ ID NO: 3) encoding human superoxide dismutase 1, soluble wherein the compound specifically hybridizes with and inhibits expression of human superoxide dismutase 1 and wherein the compound is an antisense compound, wherein the antisense oligonucleotide comprises a modified phosphorothioate linkage, a 2'-O-methoxyethyl sugar moiety or a modified nucleobase (i.e. 5-methylcytosine) or chimeras.

Stinchcomb et al. is relied upon for the reasons stated above. Stinchcomb et al. do not teach antisense sequences comprising 5-methylcytosine nucleobase modifications or chimeras.

Baracchini et al. teach that antisense oligonucleotides can be used for research purposes, and also teach that preferred antisense oligonucleotides are modified in their nucleobase composition (col. 6). Baracchini teaches that such modifications are desirable in antisense oligos because these modifications have desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. Baracchini et al provide specific embodiments of such modifications at columns 6-8 and in Example 1. These specific examples taught by Baracchini et al include the presently claimed 5-methylcytosine and chimeric oligonucleotides. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture. Table 1 exemplifies the successful practice of general antisense design taught at columns 8-10. Baracchini et al. also teaches at column 8 that antisense oligonucleotides are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length. Baracchini is considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

The teachings of Bennett et al. are considered to parallel those of Baracchini *et al.* Bennett et al. teaches general antisense targeting guidelines at columns 3-4. Bennett teaches, in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics. Bennett et al. also teach one of ordinary skill to modify nucleobases in antisense oligonucleotides, including the teaching of 5-methylcytosine (col. 8-9), and also to use chimeric antisense oligonucleotides (col. 9-10). Bennett et al. teach that the above modifications are

known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. Table 1 teaches the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides. Thus, Bennett et al. is also considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

It would have been obvious to one of ordinary skill in the art to incorporate modifications as taught by Baracchini et al. and Bennett et al. into said antisense compounds, as taught by Huang et al.

One would have been motivated to create such compounds because Stinchcomb et al. expressly teach an antisense compound targeted human superoxide dismutase 1, soluble (applicants' SEQ ID NO: 3). One would have been motivated to modify said antisense compounds as taught by Baracchini et al. and Bennett et al., because both teach that such modifications increase an antisense compound's cellular uptake, target affinity and resistance to degradation. Further, one would have been motivated to create and modify such compounds because Bennett et al. teach antisense compounds that specifically target a desired gene can be used to elucidate the function of the particular gene.

Finally, one would have a reasonable expectation of success because Baracchini et al. and Bennett et al. both teach making modified antisense compounds targeted to distinct regions of a target gene, the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as

general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635

SEAN McGARRY
PRIMARY EXAMINER
1635

ATTACHMENT TO OFFICIAL ACTION


```
;    APPLICANT:  Stinchcomb, Daniel T.
;    APPLICANT:  Jarvis, Thale
;    APPLICANT:  McSwiggen, James
;    TITLE OF INVENTION:  METHOD AND REAGENT FOR THE
;    TITLE OF INVENTION:  INDUCTION OF GRAFT TOLERANCE
;    TITLE OF INVENTION:  AND REVERSAL OF IMMUNE RESPONSES
;    NUMBER OF SEQUENCES:  2751
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Lyon & Lyon
;      STREET:  633 West Fifth Street
;      STREET:  Suite 4700
;      CITY:  Los Angeles
;      STATE:  California
;      COUNTRY:  U.S.A.
;      ZIP:  90071
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  3.5" Diskette, 1.44 Mb
;      MEDIUM TYPE:  storage
;      COMPUTER:  IBM Compatible
;      OPERATING SYSTEM:  IBM P.C. DOS 5.0
;      SOFTWARE:  FastSEQ Version 1.5
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/585,684B
;      FILING DATE:  January 16, 1996
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  60/000,951
;      FILING DATE:  July 7, 1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Warburg, Richard
;      REGISTRATION NUMBER:  32,327
;      REFERENCE/DOCKET NUMBER:  218/078
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (213) 489-1600
;      TELEFAX:  (213) 955-0440
;      TELEX:  67-3510
;  INFORMATION FOR SEQ ID NO:  2103:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  15 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
US-08-585-684B-2103

  Query Match             1.4%;  Score 12;  DB 1;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 37;
  Matches   12;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         431 AAAGCAGATGAC 442
               ||||||||||||
Db          14 AAAGCAGATGAC 3


RESULT 55
US-09-038-073-2103/c
; Sequence 2103, Application US/09038073
; Patent No. 6194150
;  GENERAL INFORMATION:
;    APPLICANT:  Stinchcomb, Daniel T.
;    APPLICANT:  Jarvis, Thale
;    APPLICANT:  McSwiggen, James
;    TITLE OF INVENTION:  METHOD AND REAGENT FOR THE
;    TITLE OF INVENTION:  INDUCTION OF GRAFT TOLERANCE
;    TITLE OF INVENTION:  AND REVERSAL OF IMMUNE RESPONSES
;    NUMBER OF SEQUENCES:  2751
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Lyon & Lyon
;      STREET:  633 West Fifth Street
;      STREET:  Suite 4700
;      CITY:  Los Angeles
;      STATE:  California
;      COUNTRY:  U.S.A.
;      ZIP:  90071
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  3.5" Diskette, 1.44 Mb
;      MEDIUM TYPE:  storage
;      COMPUTER:  IBM Compatible
;      OPERATING SYSTEM:  IBM P.C. DOS 5.0
;      SOFTWARE:  FastSEQ Version 1.5
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/09/038,073
;      FILING DATE:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/585,684
;      FILING DATE:
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Warburg, Richard
;      REGISTRATION NUMBER:  32,327
;      REFERENCE/DOCKET NUMBER:  218/078
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (213) 489-1600
;      TELEFAX:  (213) 955-0440
;      TELEX:  67-3510
;  INFORMATION FOR SEQ ID NO:  2103:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  15 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
US-09-038-073-2103

  Query Match             1.4%;  Score 12;  DB 1;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 37;
  Matches   12;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         431 AAAGCAGATGAC 442
               ||||||||||||
Db          14 AAAGCAGATGAC 3


Search completed: April 14, 2005, 16:47:12
Job time : 0.001 secs
```

```
XX
PS   Example 4; SEQ ID NO 15; 61pp; English.
XX
CC   The present sequence is a human superoxide dismutase (SOD1) wild-type
CC   sequence, which was used to demonstrate the method of the invention. The
CC   invention provides methods of specifically inhibiting the expression of a
CC   mutant allele, while preserving the expression of a co-expressed wild-
CC   type allele, using RNA interference (RNAi). The methods are useful for
CC   treating a subject having a disorder correlated with the presence of a
CC   dominant gain of function mutant allele, e.g. amyotrophic lateral
CC   sclerosis (ALS, caused by SOD mutation), Huntington's disease,
CC   Alzheimer's disease, and Parkinson's disease (claimed). To test whether
CC   small hairpin RNA (shRNA) can selectively block the expression of a
CC   mutant but not wild-type SOD1 expression, a plasmid was constructed that
CC   synthesised an shRNA ADO43056 homologous to a disease-causing mutant
CC   SOD1, G93A (nucleotide change from G to C at nucleotide position 281,
CC   placing a G:G mismatch at selective sites between the shRNA and wild-type
CC   SOD1) under the control of a RNA polymerase III promoter. Results showed
CC   that when co-transfected with either wild-type or mutant SOD1-GFP
CC   plasmids, this construct triggered single-nucleotide selective RNAi of
CC   mutant SOD1 in cultured cells.
XX
SQ   Sequence 35 BP; 8 A; 6 C; 11 G; 10 T; 0 U; 0 Other;

  Query Match             4.0%;  Score 35;  DB 1;  Length 35;
  Best Local Similarity   100.0%;  Pred. No. 5.1;
  Matches   35;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        329 ACTGCTGACAAAGATGGTGTGGCCGATGTGTCTAT 363
              |||||||||||||||||||||||||||||||||||
Db          1 ACTGCTGACAAAGATGGTGTGGCCGATGTGTCTAT 35


RESULT 10
ABK66923
ID   ABK66923 standard; DNA; 28 BP.
XX
AC   ABK66923;
XX
DT   02-JUL-2002  (first entry)
XX
DE   Human gene specific PCR primer #1011.
XX
KW   Primer; ss; DNA microarray; differential expression analysis; human.
XX
OS   Homo sapiens.
XX
PN   US6352829-B1.
XX
PD   05-MAR-2002.
XX
PF   05-JAN-1999;   99US-00225928.
XX
PR   21-MAY-1997;   97US-00859998.
XX
PA   (CLON-) CLONTECH LAB INC.
XX
PI   Chenchik A,  Jokhadze G,  Bibilashvilli R;
XX
DR   WPI; 2002-314699/35.
XX
PT   Producing sub-population of labeled nucleic acids, useful for analyzing
PT   differences in RNA profiles between several different physiological
PT   sources, using set of distinct gene specific primers.
XX
PS   Example 3; SEQ ID NO 1011; 11pp; English.
XX
CC   The invention relates to producing a sub-population of labeled nucleic
CC   acids (NAs) comprising contacting a NA sample from a physiological
CC   source, with a pool of 50 distinct gene specific primers under suitable
CC   conditions to enzymatically generate sub-population of NAs, where each
CC   gene specific primer has a sequence complementary to a distinct mRNA, and
CC   each labeled NA is generated using a single gene specific primer. The
CC   method is useful for producing a sub-population of labeled NAs which is
CC   useful for analysing the differences in the RNA profiles between several
CC   different physiological sources, where the method comprises producing
CC   subpopulation of labeled NAs for the different physiological sources,
CC   comprising the populations for each physiological source to identify
CC   differences in the population, where the comparison is preferably
CC   performed by hybridising the labeled NAs for each of the distinct
CC   physiological sources to an array of probe NAs stably associated with the
CC   surface of a substrate to produce a hybridisation pattern for each of the
CC   sources, and comparing the patterns for each of the sources, where
CC   differential gene expression assays are utilised in differential
CC   expression analysis of diseased a normal tissue e.g. neoplastic a normal
CC   tissue, or different tissue or subtissue types. The present sequence is a
CC   human gene specific PCR primer used in the method of the invention. Note:
CC   The sequence data for this patent did not form part of the printed
CC   specification, but was obtained in electronic format directly from USPTO
CC   at http.wipo.seqdata.uspto.gov/sequence.html?DocID=6352829B1
XX
SQ   Sequence 28 BP; 8 A; 6 C; 8 G; 6 T; 0 U; 0 Other;

  Query Match             3.2%;  Score 28;  DB 1;  Length 28;
  Best Local Similarity   100.0%;  Pred. No. 17;
  Matches   28;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        106 AGTGCAGGGCATCATCAATTTCGAGCAG 133
              ||||||||||||||||||||||||||||
Db          1 AGTGCAGGGCATCATCAATTTCGAGCAG 28


RESULT 11
ABK66924/c
ID   ABK66924 standard; DNA; 28 BP.
XX
AC   ABK66924;
XX
DT   02-JUL-2002  (first entry)
XX
DE   Human gene specific PCR primer #1012.
XX
KW   Primer; ss; DNA microarray; differential expression analysis; human.
XX
OS   Homo sapiens.
XX
PN   US6352829-B1.
XX
PD   05-MAR-2002.
XX
PF   05-JAN-1999;   99US-00225928.
XX
PR   21-MAY-1997;   97US-00859998.
XX
PA   (CLON-) CLONTECH LAB INC.
XX
PI   Chenchik A,  Jokhadze G,  Bibilashvilli R;
XX
DR   WPI; 2002-314699/35.
XX
PT   Producing sub-population of labeled nucleic acids, useful for analyzing
PT   differences in RNA profiles between several different physiological
PT   sources, using set of distinct gene specific primers.
XX
PS   Example 3; SEQ ID NO 1012; 11pp; English.
XX
CC   The invention relates to producing a sub-population of labeled nucleic
CC   acids (NAs) comprising contacting a NA sample from a physiological
CC   source, with a pool of 50 distinct gene specific primers under suitable
CC   conditions to enzymatically generate sub-population of NAs, where each
CC   gene specific primer has a sequence complementary to a distinct mRNA, and
CC   each labeled NA is generated using a single gene specific primer. The
CC   method is useful for producing a sub-population of labeled NAs which is
CC   useful for analysing the differences in the RNA profiles between several
CC   different physiological sources, where the method comprises producing
CC   subpopulation of labeled NAs for the different physiological sources,
```

```
XX
PD   31-JUL-1992.
XX
PF   11-DEC-1990;   90JP-00401323.
XX
PR   11-DEC-1990;   90JP-00401323.
XX
PA   (SUNR ) SUNTORY LTD.
PA   (INOU/) INOUE M.
XX
DR   WPI; 1992-304666/37.
XX
PT   New hypotensive agents - comprise superoxidedismutase with attached
PT   heparin binding site.
XX
PS   Disclosure; Page 4; 9pp; Japanese.
XX
CC   The sequences given in AAQ27817-20 are primers which were used to amplify
CC   the superoxidase dismutase (SOD) gene which is used in the production of
CC   a new hypotensive agent. The amplification product of these reactions is
CC   ligated to a heparin binding site (HBS). SOD does not naturally contain
CC   an HBS. This new construct can exert hypotensive activity in vivo as the
CC   active component can be concentrated in the blood vessel endothelial
CC   cells
XX
SQ   Sequence 40 BP; 14 A; 6 C; 12 G; 8 T; 0 U; 0 Other;

  Query Match             4.6%;  Score 40;  DB 1;  Length 40;
  Best Local Similarity   100.0%;  Pred. No. 2.1;
  Matches   40;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        464 GAAAGTACAAAGACAGGAAACGCTGGAAGTCGTTTGGCTT 503
              ||||||||||||||||||||||||||||||||||||||||
Db          1 GAAAGTACAAAGACAGGAAACGCTGGAAGTCGTTTGGCTT 40


RESULT 8
ADE52418
ID   ADE52418 standard; DNA; 35 BP.
XX
AC   ADE52418;
XX
DT   29-JAN-2004  (first entry)
XX
DE   Wild-type human SOD1 partial DNA sequence.
XX
KW   Suppression of gene expression; eukaryotic cell; RNA polymerase promoter;
KW   target DNA sequence; RNA polymerase termination signal;
KW   hairpin structure; RNA polymerase III; RNA Pol III; mutated protein;
KW   cancer; leukaemia; haemophilia; viral infection; bacterial infection;
KW   neurodegenerative disease; Alzheimer's disease; Parkinson's disease;
KW   Huntington's disease; amyotrophic lateral sclerosis; ALS; cytostatic;
KW   haemostatic; virucide; antibacterial; neuroprotective; nootropic;
KW   anticonvulsant; antiparkinsonian; human; superoxide dismutase 1; SOD1;
KW   ds.
XX
OS   Homo sapiens.
XX
PN   US2003180756-A1.
XX
PD   25-SEP-2003.
XX
PF   21-NOV-2002; 2002US-00301516.
XX
PR   21-MAR-2002; 2002US-0366478P.
XX
PA   (SHIY/) SHI Y.
PA   (SUIG/) SUI G.
XX
PI   Shi Y,  Sui G;
XX
DR   WPI; 2003-852231/79.
XX
PT   New nucleic acids, useful for inhibiting the synthesis of a target
PT   protein in a eukaryotic cell, or for treating various diseases by
PT   inhibiting the expression of abnormal or mutated proteins, e.g. leukemia,
PT   viral or bacterial infection.
XX
PS   Example 6; Fig 7A; 38pp; English.
XX
CC   The present invention relates to a method for suppressing gene expression
CC   in cells, particularly eukaryotic cells. The method involves a new
CC   nucleic acid comprising in a 5'-3' order: an RNA polymerase promoter
CC   sequence, a first target sequence that is essentially complementary to a
CC   sequence of a target nucleic acid or its complement, a spacer sequence, a
CC   second target sequence that is essentially complementary to the first
CC   target sequence, and an RNA polymerase termination signal, where an RNA
CC   transcribed from the nucleic acid can inhibit expression of the target
CC   gene. The RNA transcribed from the nucleic acid may form a hairpin
CC   structure. The polymerase is preferably RNA polymerase III (Pol III) and
CC   the polymerase termination signal comprises a number of thymidines
CC   sufficient for arresting Pol III activity. The nucleic acids and methods
CC   are useful for suppressing gene expression in cells, or inhibiting the
CC   synthesis of a target protein in a eukaryotic cell or in a cell of a
CC   subject. The nucleic acids can be used for treating various diseases by
CC   inhibiting the expression of abnormal or mutated proteins, e.g. cancers
CC   such as leukaemia, haemophilia, viral or bacterial infections, and
CC   neurodegenerative diseases including Alzheimer's disease, Parkinson's
CC   disease, Huntington's disease and amyotrophic lateral sclerosis (ALS).
CC   The present sequence represents a partial DNA sequence from the wild-type
CC   human superoxide dismutase 1 (SOD1) gene.
XX
SQ   Sequence 35 BP; 8 A; 6 C; 11 G; 10 T; 0 U; 0 Other;

  Query Match             4.0%;  Score 35;  DB 1;  Length 35;
  Best Local Similarity   100.0%;  Pred. No. 5.1;
  Matches   35;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        329 ACTGCTGACAAAGATGGTGTGGCCGATGTGTCTAT 363
              |||||||||||||||||||||||||||||||||||
Db          1 ACTGCTGACAAAGATGGTGTGGCCGATGTGTCTAT 35


RESULT 9
ADO43055
ID   ADO43055 standard; mRNA; 35 BP.
XX
AC   ADO43055;
XX
DT   12-AUG-2004  (first entry)
XX
DE   Superoxide dismutase wild-type target for RNA interference.
XX
KW   Superoxide dismutase; SOD; enzyme; amyotrophic lateral sclerosis;
KW   RNA interference; gene silencing; human; ss.
XX
OS   Homo sapiens.
XX
PN   WO2004042027-A2.
XX
PD   21-MAY-2004.
XX
PF   04-NOV-2003; 2003WO-US035009.
XX
PR   04-NOV-2002; 2002US-0423507P.
PR   18-JUL-2003; 2003US-0488283P.
XX
PA   (UYMA-) UNIV MASSACHUSETTS.
XX
PI   Xu Z,  Zamore PD;
XX
DR   WPI; 2004-390611/36.
XX
PT   Inhibiting expression of a target allele in a cell comprising at least
PT   two different alleles of a gene, for treating CNS disorders, comprises
PT   administering to the cell an siRNA specific for the target allele.
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